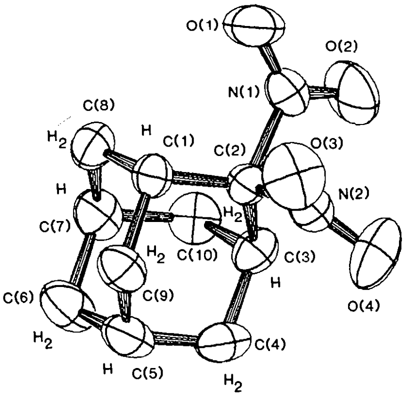

Fig. 2. A representation of the molecular structure and thermal motion of 2,2-dinitroadamantane (II). Thermal ellipsoids are at the 50% probability level.

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Structure of (±)-Methyl 7,7-Ethylenedioxy-*cis*-4a,5,6,7,8,8a-hexahydro-4a-coumarincarboxylate, $C_{13}H_{16}O_6$, and the Configuration of the 1,3-Dioxolane Ring

By Clara Brink Shoemaker, David P. Shoemaker, Sarah L. Barkowski, Richard J. French and M. Rahim Kazerouni

Department of Chemistry, Oregon State University, Corvallis, Oregon 97331, *USA*

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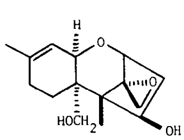
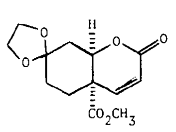
Abstract. $M_r = 268{\cdot}27$, monoclinic, $P2_1/n$, $a = 13{\cdot}296\,(6)$, $b = 15{\cdot}143\,(5)$, $c = 6{\cdot}288\,(2)$ Å, $\beta = 98{\cdot}89\,(3)°$, $V = 1250{\cdot}8\,(9)$ Å^3, $Z = 4$, $D_m = 1{\cdot}405$, $D_x = 1{\cdot}425$ g cm^{-3}, $\lambda(\text{Mo } K\alpha) = 0{\cdot}71069$ Å, $\mu = 1{\cdot}06$ cm^{-1}, $F(000) = 568$, $T = 293\,(2)$ K. Final $R = 0{\cdot}052$ for 2052 observed reflections. The compound is a precursor to the anti-tumor agent verrucarol and related verrucarins (antibiotic substances isolated from a soil fungus). The X-ray study confirmed the *cis* configuration of the H atom at C(8a) and the methoxycarbonyl group at C(4a). The configuration of the ethylenedioxy (1,3-dioxolane) group is between an envelope and a twist, but closer to a twist; comparisons with the configurations of this group in other structures are presented.

Introduction. The verrucarins, a family of antibiotic substances isolated from the soil fungus *Myrothecium verrucaria* are among the most active cytostatic agents known (Tamm, 1974). A common unit found in the structures of these complex metabolites is the sesquiterpene verrucarol (I).



(I)



(II)

Approaches to the synthesis of (I) are in progress in the laboratory of J. D. White of this University (White, Matsui & Thomas, 1981; White, Carter & Kezar, 1982). In the course of these studies, it became important to establish that a key intermediate, lactone (II), possesses the *cis* ring fusion shown. Since this configuration will ultimately appear in (I) and since the

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method of synthesis of (II) was not entirely unambiguous with respect to this stereochemical point (White & Hill, 1983), the crystal structure of (II), the title compound, was determined. It was also of interest to examine the configuration of the 1,3-dioxolane ring, which is present as the ethylenedioxy substituent group.

Experimental. Colorless, prismatic crystal, recrystallized from methanol, approximate dimensions 0·2 × 0·3 × 0·5 mm. D_m measured by flotation in CCl_4/hexane. Syntex $P\bar{1}$ diffractometer, graphite monochromator, Mo $K\alpha$ radiation, θ–2θ scan speed 1° $\min^{-1}$, 2θ range 2·0° plus α_1,α_2 angular separation. 15 reflections used for measuring lattice parameters. Ratio of background time to scan time 1:2, a quarter sphere of reciprocal space measured (h 0–17, k −8–8, l 0–19), $2\theta_{\max} = 55°$. Three standard reflections, intensity variation ±5%. 2900 unique reflections, 2063 with $F^2 > 2\sigma$ used in refinement. In final cycles 11 strongest reflections, apparently affected by secondary extinction, given zero weight. $R_{\text{int}} = 0{\cdot}013$. No absorption correction. Structure solved by direct-methods program *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) with 176 E values >1·2 and 1071 phase relationships. E maps, calculated with set of phases with highest combined figure of merit (RESID = 17·10), revealed all 19 non-H atoms as the 19 strongest peaks. After full-matrix least-squares refinement of C and O parameters, first with isotropic and then anisotropic thermal parameters, to $R = 0{\cdot}098$, all 16 H atoms revealed as the 16 strongest peaks on a difference Fourier map. Two cycles of refinement performed varying positional coordinates and isotropic thermal parameters of H atoms, and anisotropic thermal parameters of C and O atoms, but not their positional coordinates (179 parameters); three more cycles, in which H atoms fixed and positional and anisotropic thermal parameters of C and O atoms varied (172 parameters), led to a final $R = 0{\cdot}052$ (2052 reflections), $R_w = 0{\cdot}048$, $S = 2{\cdot}32$. Least-squares program used was Zalkin's (undated), quantity minimized $\sum w(|F_o| - |F_c|)^2$ with $w^{-1} = C + Bt^2 + [0{\cdot}02(C - Bt)]^2$ (C is the integrated count; B is the total background count; t, which has the value 2, is the ratio of scan time to background time). $(\Delta/\sigma)_{\max} = 0{\cdot}06$, $(\Delta/\sigma)_{\text{mean}} = 0{\cdot}005$. Final $\Delta\rho$ excursions $-0{\cdot}18$–$0{\cdot}20$ e Å^{-3}. Scattering factors from *International Tables for X-ray Crystallography* (1962, 1974).

Discussion. The positional and isotropic thermal parameters of all atoms are listed in Table 1.* The numbering of the atoms, interatomic distances and angles are given in Fig. 1. A packing drawing of the structure is given in Fig. 2, and a stereoview of the molecule is given in Fig. 3.* The configuration at the ring fusion is *cis* [*i.e.* the H atom at C(8a) and the methoxycarbonyl group at C(4a) are *cis*], which makes the compound a suitable precursor for synthesis of verrucarins. The *cis* ring fusion was previously confirmed by X-ray diffraction for the verrucarin trichodermol *p*-bromobenzoate (Abrahamsson & Nilsson, 1966).

The α,β-unsaturated carbonyl group of the lactone ring is approximately planar; the deviations of atoms O(1), C(2), O(13), C(3), and C(4) from the least-squares plane are 0·022, 0·031, −0·073, 0·110, and −0·090 Å, respectively. Atoms C(4a) and C(8a) at the ring fusion are −0·353 and +0·363 Å out of this plane. In coumarin (Gavuzzo, Mazza & Giglio, 1974), the lactone ring is fused to a benzene ring and all main skeleton atoms are within 0·015 Å of a least-squares

Table 1. *Positional parameters* (×10^5, *for* H ×10^4) *and isotropic thermal parameters with e.s.d.'s*

For non-H atoms, B_{eq} is the arithmetic mean of the principal axes of the thermal ellipsoids. The e.s.d. in B_{eq} is about 0·10 Å^2 for C and 0·07 Å^2 for O.

	x	y	z	B_{eq}/B(Å^2)
C(2)	29945 (16)	31625 (13)	37350 (34)	3·20
C(3)	36594 (16)	27887 (13)	55980 (31)	3·25
C(4)	45414 (15)	24157 (12)	54074 (29)	2·89
C(4a)	49099 (14)	23997 (12)	32475 (28)	2·59
C(5)	60837 (14)	23880 (13)	34516 (33)	3·34
C(6)	65591 (15)	32580 (14)	43231 (36)	3·95
C(7)	61315 (16)	40179 (14)	29161 (35)	3·65
C(8)	49915 (15)	40772 (12)	28152 (32)	3·21
C(8a)	44909 (14)	32132 (12)	19612 (29)	2·70
C(9)	45321 (14)	15646 (12)	20110 (31)	2·74
C(10)	72101 (19)	44441 (17)	5850 (46)	5·39
C(11)	71609 (22)	51643 (18)	21846 (41)	5·60
C(12)	41470 (20)	460 (14)	23607 (39)	4·64
O(1)	33921 (10)	32833 (9)	18931 (21)	3·20
O(13)	21102 (11)	33385 (11)	37215 (26)	4·71
O(14)	63341 (12)	39225 (10)	7669 (26)	4·84
O(15)	66011 (12)	48234 (10)	37108 (28)	5·08
O(16)	43177 (13)	15153 (10)	1020 (22)	4·39
O(17)	44867 (12)	8876 (9)	33338 (22)	4·17
H(3)	3370 (22)	2785 (20)	7082 (48)	5·3 (7)
H(4)	4986 (22)	2107 (18)	6801 (45)	4·7 (7)
H(51)	6302 (23)	1916 (19)	4452 (48)	4·3 (7)
H(52)	6315 (24)	2227 (21)	1930 (52)	6·0 (8)
H(61)	7283 (24)	3209 (20)	4251 (50)	5·5 (8)
H(62)	6422 (25)	3436 (21)	5880 (51)	6·2 (8)
H(81)	4829 (20)	4192 (17)	4317 (44)	3·8 (6)
H(82)	4727 (23)	4601 (19)	1806 (46)	5·0 (7)
H(8a)	4588 (24)	3123 (20)	334 (51)	3·6 (8)
H(101)	2817 (29)	862 (24)	6207 (62)	8·6 (1·0)
H(102)	7177 (29)	4693 (24)	9059 (59)	7·7 (1·0)
H(111)	3332 (33)	4316 (28)	8511 (68)	11·8 (1·2)
H(112)	7154 (35)	460 (29)	2023 (67)	14·2 (1·3)
H(121)	3497 (27)	119 (23)	1388 (54)	6·9 (9)
H(122)	5312 (30)	175 (25)	8310 (60)	8·5 (1·1)
H(123)	5997 (27)	287 (23)	6316 (55)	7·2 (9)

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* Lists of structure factors, anisotropic thermal parameters, and bond lengths and angles involving H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38774 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

* Molecule (1) in Fig. 3, with coordinates given in Table 1, is the enantiomer derived from *MULTAN*. The configuration of this segment in the verrucarins [see formula (II) in the *Introduction*] corresponds, however, to the enantiomer ($\bar{1}$) in Fig. 2.

plane. Our bond distances in the unsaturated carbonyl group agree to within 0·02 Å with those determined for coumarin.

The saturated ring C(4a),C(5),C(6),C(7),C(8),C(8a) has the chair configuration. The ethylenedioxy (1,3-dioxolane) ring is non-planar; the deviations of the atoms from the least-squares plane are given in Fig. 4, together with the torsion angles.

The pucker in the 1,3-dioxolane ring may be described by a pseudorotation angle P and a maximum torsion angle $\varphi_{\max}$ (Altona, Geise & Romers, 1968; Altona & Sundaralingam, 1972). In Table 2 these angles are defined and listed for the present compound and for some other 2-substituted 1,3-dioxolane groups. P for the present compound is 30°, *i.e.* the shape of the ring is between an envelope ($P = 18°$) with approximate mirror symmetry with respect only to the displacements of the atoms from a plane [in the numbering scheme of Fig. 4: atom (5) out of the plane of atoms (1)–(4)], and a twist ($P = 36°$) with an approximate twofold axis [passing through atom (3) and the midpoint of the (1)–(5) bond], but somewhat closer to a twist. Similar shapes of this ring have been reported in a centrosymmetric molecule with two 1,3-dioxolane groups attached at their 2-positions to a cyclohexane ring (Chadwick, Dunitz & Schweizer, 1977), and in a compound with this group attached similarly to a substituted decalin group (Chadwick & Dunitz, 1978). The shape of the ring in these compounds (see Table 2) is between an envelope [atom (4) out of the plane of the other four atoms] and a twist [with approximate twofold axis passing through atom (1)]. In a compound with the 1,3-dioxolane group attached at its 2-position to a pyrrolidine ring (Sheldrick, Borkenstein & Engel, 1978), the shape is between an envelope [with atom (1),

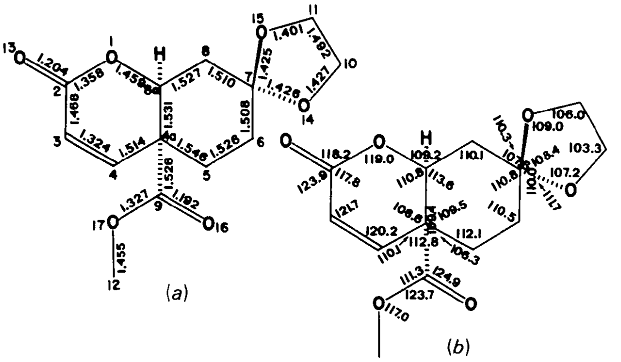

Fig. 1. (*a*) Numbering scheme and bond distances (Å) and (*b*) angles (°). The e.s.d.'s on the distances and angles (excluding H atoms), as calculated by Zalkin's (undated) *DISMAT* program, are ≤0·004 Å and ≤0·20°.

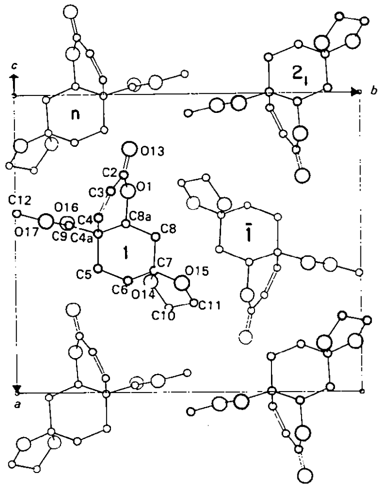

Fig. 2. Packing diagram: projection normal to the *a*,*b* plane of molecule (1) (with coordinates as given in Table 1) and the molecules related to it by the symmetry center ($\bar{1}$) at $\frac{1}{2}\frac{1}{2}0$, the n glide at $y = \frac{1}{4}$ and the 2_1 axes at $z = \frac{1}{4}$.

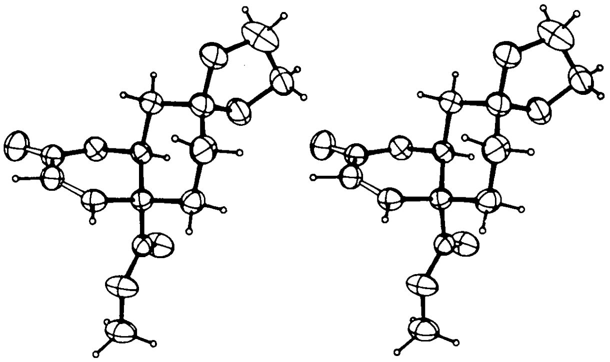

Fig. 3. *ORTEP*II (Johnson, 1976) stereoscopic drawing of molecule (1) of Fig. 2. The orientation is obtained from that shown in Fig. 2 by (i) rotating the molecule by −30° about an axis parallel to the b axis of Fig. 2, followed by (ii) rotating the molecule by +90° about an axis (toward the viewer) perpendicular to the plane of Fig. 2. C and O atoms are shown as 50% probability ellipsoids; H atoms are shown as spheres of arbitrary size. [See footnote in text regarding enantiomer portrayed.]

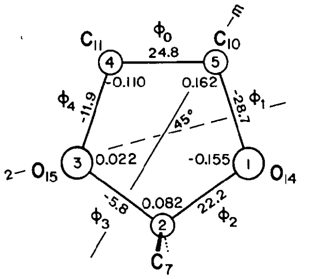

Fig. 4. The 1,3-dioxolane ring (idealized as a regular pentagon), showing the deviations z from the least-squares plane (Å), the torsion angles φ (°), and the positions of the twofold axis (2) and the mirror (m) in the approximate deviation function: $z = (0{\cdot}17\text{ Å}) \cos 2(\theta - 30°)$, where θ is measured clockwise around the ring from the center of the C—C bond. The corresponding approximate function for the torsion angle is: $\varphi = 29° \times \cos 2(\theta + 15°)$, 15° being $P/2$ where $P = 30°$ is given in Table 2.

oxygen in this case, out of the plane of the other four atoms] and a twist [with the approximate twofold axis passing through atom (3)]. In 2,2′-bi-1,3-dioxolane (Furberg & Hassel, 1950; Altona & VanderVeek, 1968), the shape of the ring is somewhat closer to an envelope (this is the only one of the compounds considered here in which the 2-position is not spiro). Epe, Rösner & Tochtermann (1980) have described a compound with this group attached to a cycloheptane ring; there are two independent molecules, *A* and *B*, in the asymmetric unit. We found that for both molecules the shape of the ring is close to an envelope with atom (2) out of the plane of the other four atoms. Similarly, Declercq, Germain, Van Meerssche, Devreese, Declercq & Vandewalle (1981) found in a compound which also has the 1,3-dioxolane ring attached in its 2-position to a cycloheptane ring, that the shape is an almost perfect envelope. In a derivative of the quebrachamine family of indole derivatives described by Sundberg, Luis, Parton, Schreiber, Srinivasan, Lamb, Forcier & Bryan (1978), the two independent molecules in the asymmetric unit have a different conformation for the 1,3-dioxolane ring which is attached to a nine-membered ring. In one molecule the conformation is close to an envelope and in the other molecule it is close to a twist, showing the influence of different packing environments on the conformations of otherwise identical molecules. The energy difference between the C_s and C_2 forms is apparently small.

The molecule 1,3-dioxolane itself shows essentially free pseudorotation in the gas phase, as determined from the far-IR spectrum by Greenhouse & Strauss (1969) and the microwave spectrum by Baron & Harris (1974). In the crystallized compounds considered here, substituents on the dioxolane ring at the 2-position and packing effects from the surrounding molecules lead to forms between approximate C_s and C_2 symmetries.

Table 2. *Maximum torsion angles $\varphi_{\max}$ and pseudorotation angles P (°) in some 2-substituted* 1,3-*dioxolane groups* (*see text*)

The angles are defined (Altona & Sundaralingam, 1972; see Fig. 4) by: $\tan P = |(\varphi_2 + \varphi_4) - (\varphi_1 + \varphi_3)|/2\varphi_0(\sin 36° + \sin 72°)$, $\varphi_{\max} = \varphi_0/\cos P$. P (mod 367) = 0° for twist (2) and = 18° for envelope (*m*).

Reference	$\varphi_{\max}$	P (mod 36°)	Fig. 4 atom No. at nearest approx.		Best description
			2	*m*	
This study	29	30	O(3)	C(5)	Twist
Chadwick *et al.* (1977)	32	7	O(1)	C(4)	(Twist)
Chadwick & Dunitz (1978)	32	8	O(1)	C(4)	(Twist)
Sheldrick *et al.* (1978)	29	8	O(3)	O(1)	(Twist)
Furberg & Hassel (1950); Altona & VanderVeek (1968)	30	25	O(1)	O(3)	(Envelope)
Epe *et al.* (1980) *A*	35	21	C(5)	C(2)	Envelope
B	34	22	C(5)	C(2)	Envelope
Declercq *et al.* (1981)	25	18		C(2)	Envelope

The shortest intermolecular distances between non-H atoms are: C(12)···O(13), 3·097; O(13)···O(15), 3·526; C(12)···C(10), 3·599 Å.

This structure determination was a class project in a graduate course on X-ray crystallography taught by the two senior authors. We thank Professor J. D. White, of this Department, for suggesting the problem and for valuable discussions, and David E. Hill for providing the compound. Computing costs were supported in part by the OSU Computer Center and in part by the National Institutes of Health under Grant No. AI10964.

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